Metabolism of other hexoses

By the end of these lectures you would be able to: -

1. Identify different metabolic pathways of fructose metabolism
2. Relate abnormal fructose metabolism to clinical disorders
3. Corelate abnormal galactose metabolism to clinical disorders

I- Fructose metabolism:

- A Monosaccharide (ketohexose) that occurs in significant amounts in diet (1ry in disaccharides).

Sources Of Fructose:

1- Disaccharide sucrose: (major source) , cleaved in the intestine, releases fructose & glucose.

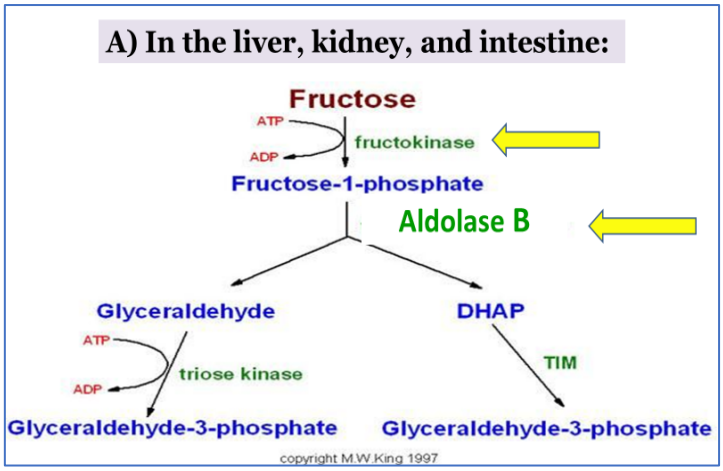
2- Found as a Free monosaccharide:

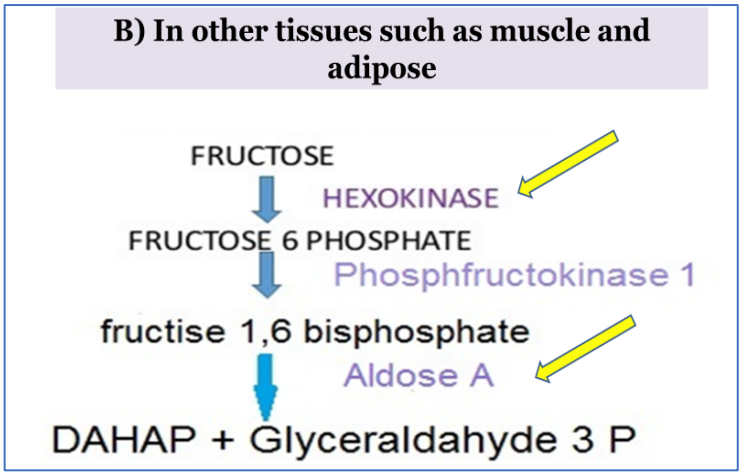
- Fruits
- Honey
- High-fructose corn Syrup (55% fructose/45% glucose typically), which is used to sweeten Soft drinks & many foods.

3- Fructose can arise from glucose inside the body via sorbitol (polyol) pathway in some tissues, In Seminal vesicles: is for benefit of sperm cells, which use fructose as a major carbohydrate energy source.

Fructose metabolism

- Fructose to enter the pathways of intermediary metabolism, it must first be phosphorylated by either **hexokinase** or **fructokinase.**
- **Fructokinase** provides the primary mechanism for fructose phosphorylation. It is found in the liver (which processes most of the dietary fructose), kidney, and the small intestinal mucosa, and converts fructose to fructose1-phosphate, using ATP as the phosphate donor.
- It is the rate limiting step and it is insulin independent. Its activity depends on fructose concentration.
- **Hexokinase** has a very low affinity (high Km) for fructose.





Hereditary Fructose intolerance (Fructose induced hypoglycemia):

Result from **aldolase B deficiency** causing:

- Fructose 1-phosphate accumulates, resulting in a drop in the level of inorganic phosphate (Pi) and, therefore, of ATP. As ATP falls, AMP rises.
- Increased Fructose 1-phosphate Inhibit glycogen phosphorylase causing hypoglycemia, vomiting & accumulation of glycogen in liver.
- In the absence of Pi, AMP is degraded, causing hyperuricemia and lactic acidosis.
- The decreased availability of hepatic ATP affects gluconeogenesis (causing hypoglycemia with vomiting), and protein synthesis (causing a decrease in blood clotting factors and other essential proteins).
- Kidney function may also be affected.

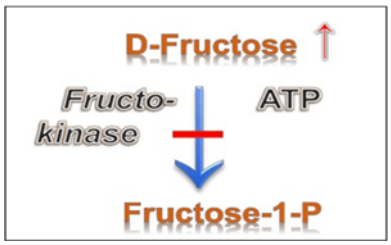
Diagnosis of HFI:

- Can be made on the basis of fructose in the urine, enzyme assay or by DNA-based testing.

Treatment of HFI:

- Sucrose as well as fructose, must be removed from the diet to prevent liver failure & possible death.

Essential Fructosuria



- Autosomal recessive disorder (1:130,000).
- Caused by a deficiency of the hepatic fructokinase enzyme, fructose is not metabolized in the liver.
- Fructose is either excreted unchanged in the urine or metabolized to F-6-P by hexokinase in adipose tissue and muscles.
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- No treatment is indicated.

II- Galactose metabolism

Different sources of galactose:

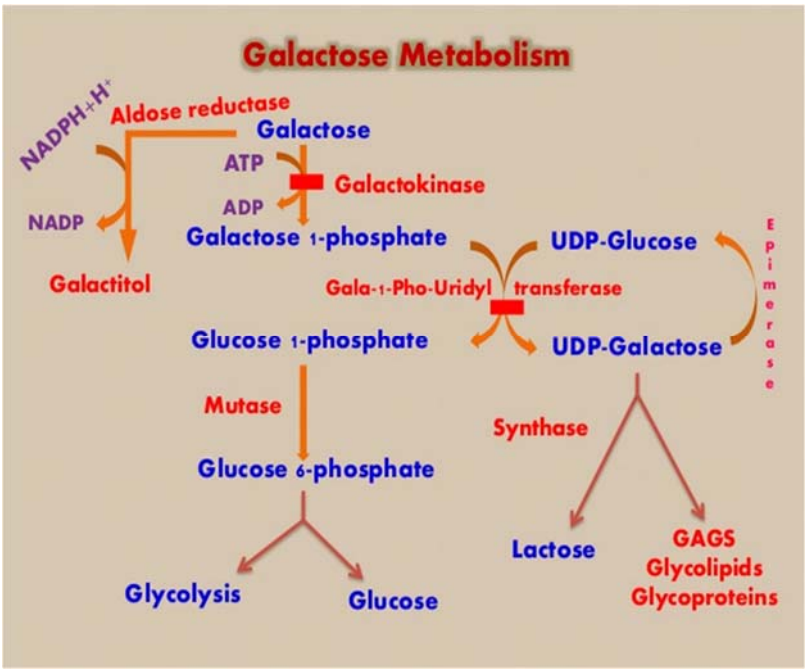
- Major dietary source of galactose is obtained from milk & milk products.

  (digestion of lactose by lactase in SI yield glucose & galactose).

- Some galactose can also be obtained by lysosomal degradation of complex carbohydrates (glycoproteins & glycolipids).
- Most tissues have a specific enzyme for this purpose, galactokinase, which produces galactose 1-phosphate.

Galactose metabolism:

1. Galactose must be phosphorylated before it can be further metabolized.
2. This occurs in most tissues by galactokinase enzyme producing galactose 1-phosphate.
3. Galactose 1-phosphate is first converted to UDP-galactose.
4. This occurs in an exchange reaction, in which UDP-glucose reacts with galactose 1-phosphate, producing UDP galactose and glucose 1-phosphate.
5. This is catalyzed by galactose 1-phosphate uridyl transferase (GALT) enzyme.



- **Galactose 1-phosphate uridyl-transferase** is the rate limiting step.

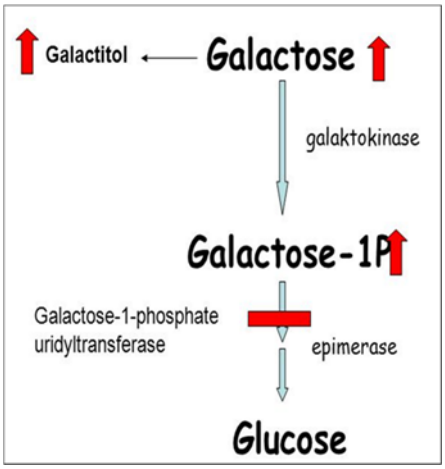
Important roles of galactose to the body :

Galactose is entering in the structure of various important molecules as:

- Glycolipids.
- Glycoproteins.
- Lactose during lactation.

Glactosemia and its biochemical basis

1- Classic galactosemia (Sever form):



- Inborn error of galactose metabolism.
- Due to deficiency of **Galactose-1-p uridyl Transferase (GALT)** enzyme.
- Galactose 1-phosphate and, galactose accumulate in cells
- Symptoms start at first days after breast feeding.

1- Accumulation of Galactose-1-phosphate and depletion of liver.

- Inorganic phosphate → Hypoglycemia and vomiting.

2- Galactose is a substrate for aldose reductase, forming galactitol, which accumulates in:

- Lens of the eye → Cataract
- Nerves → Mental Retardation
- Liver → Liver failure & jaundice
- Kidney → Renal failure

Treatment of classic galactosemia

- **The only treatment is eliminating lactose and galactose from the diet**
- Infants cannot be breast-fed and are usually fed a soy-based formula

2- Galactokinase deficiency (Mild form):

It is a mild disorder of galactosemia